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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	13

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/996,030	BUHRING ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *16-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-21* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4, 6, 8, 11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I (claims 1-15) in Paper No. 12 filed 11/24/03 is acknowledged. Claims 16-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 12. Accordingly claims 1-15 are under consideration.

Priority

2. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. The certified copies of German application number 19922863.9 filed May 19, 199 and German application number 19926879. 7 filed June 12, 1999 are acknowledged.

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on form PTO-1449 have cited the references they have not been considered.

4. The information disclosure statements filed 6/20/02 in paper #8 and filed 7/23/03 in paper #11 have been considered as to the merits before First Action.

5. The information disclosure statement filed 2/28/02 in paper #4 fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered.

6. The information disclosure statement filed 11/6/01 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. Examiner was able to retrieve most of the references cited on the PTO-1449 however items 4 and 7 were not obtained. Applicant is invited to submit EP 5596479 and Abstract 202545 to Thomas T et al. for consideration.

Specification

7. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

A. On page 3 3rd paragraph last line "from a being patient" appears to be a typo. Should the phrase read "from a patient"? Appropriate correction is required.

B. The use of trademarks is noted in this application. They should be capitalized wherever they appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks. (i.e., see page 21 – Sepharose).

Abstract

8. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The instant abstract utilizes the legal phrase "said" and in concise terms "concerns" "and/or". Please correct.

Claim Objections

9. Claim 8 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. As recited claim 8 appears to read on two different methods. Specifically claim 1 is drawn to cell binding while claim 8 analyzes hematopoiesis. The analyses of hematopoiesis does not further limit claim 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1 and 15 are vague and indefinite because it is not clear as to what reagent or reagents are being employed in the claimed methods. As recited it is not clear if the surface structure on the cells will bind one antibody, two antibodies, or only antibody 97A6. Accordingly the metes and bounds of the claims cannot be assessed. It is suggested that the claims clearly recite Applicants intended reagents in order to obviate this rejection.

B. In claims 1 and 15 the phrase "also capable of binding" is vague and indefinite. Although the phrase has defined meaning it is not clearly defined with respect to the antibody utilized to bind a surface structure on the cells. Is it Applicants' intent to mean that the contacted antibody is required to compete with the cited 97A6 antibodies in an assay method (i.e. binding at other sites on the same cell)? Is applicant claiming any binding agent that is capable of binding to the same epitope as the 97A6 antibodies (will only one antibody be employed)? Please clarify.

C. Claim 6 is indefinite in reciting that the antibody "essentially does not interact with immunoglobulins of the IgC class". This is not clear because it is not known if the antibody interacts with the immunoglobulins or not? Further, it is not known what is considered "essentially no interaction". It is suggested that Applicant eliminate the term "essentially" from the claims. Appropriate correction is required.

D. Claim 8 is vague and indefinite because it is not clear as to how the method of analyzing hematopoiesis will be conducted. The claim is dependent on claim 1 which merely binds cells. The correlation of or inclusion of the binding method of claim 1 does not further limit claim 8 because no additional steps are included and the procedure for analyzing hematopoiesis is not recited. The claim should be written to include all necessary method steps.

E. The term "usual" in claim 12 is a relative term, which renders the claim indefinite. The term "usual is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. What will be is considered usual immunological detection procedures? Please correct.

11. Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Merely, reciting the use of reagents in a process format is not considered to be a proper process claim.

The claims merely read on a preamble whereby reagents are contacted with each other but does not set forth steps of how the final assessment will be conducted. For example claim 2 is drawn to a method of detecting a cell surface structure and is dependent on claim 1. However claim 1 is merely drawn to cell binding. Therefore steps relating to the detection of the bound complex further correlated to the method of claim 1 are not provided.

Further, there are no claimed steps reciting the washing/removal of unbound material. With respect to claim 1, a separation step that removes unbound reagents from the formed complex is required. If you do not have a separation step after complex formation, it is not clear how one would distinguish materials bound from those which are merely present in solution but not bound to the material. Please add steps.

The methods recited in claims 1-15 require at least a contact step, complex formation, separation, and correlation. Please add the appropriate steps.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-6 and 8-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth the utility of antibody 97A6 produced by hybridoma deposited as No. DSM ACC 2297 to detect a single cell surface structure (phosphodiesterase/nucleotide pyrophosphatase ectoenzyme PDNP3, NPP3 or PD-Ibeta) on basophils, mast cells, precursor cells of basophils, or precursors of mast cells. Please see page 4 lines 16-18, Example 5, page 22 lines 2-7.

Therefore the written description is not commensurate in scope with the claims drawn to a method employing any and all antibodies capable of binding like or competes with antibody 97A6 (hybridoma deposited as No. DSM ACC 2297) to bind basophil and mast cells. *Vas-Cath Inc. V. Mahurkar*, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).With the exception of antibody 97A6 produced by hybridoma deposited as No. DSM ACC 2297, the skilled artisan cannot envision the detailed structure of all the possible encompassed antibodies as claimed and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The antibody itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Furthermore, In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of a compound/seq.id/etc. by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of molecules, usually defined by a sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description ...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

However, no disclosure, beyond the antibody 97A6 produced by hybridoma deposited as No. DSM ACC 2297 is made in the specification. This is insufficient to support the generic claims as provided by the Interim Written Description Guildlines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

Therefore only methods employing the isolated antibody 97A6 produced by hybridoma deposited as No. DSM ACC 2297, but not any antibodies that competes with antibody 97A6 produced by hybridoma deposited as No. DSM ACC 2297 in cell binding would meet the full breadth of the claims as required by the written description provision of 35 USC 112, first paragraph.

13. Claims 1-6 and 8-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide description of or enablement for the utility of any and every antibody population specific for binding basophils, mast cells, precursor cells of basophils, and precursors of mast cells other than antibody antibody 97A6 produced by hybridoma deposited as No. DSM ACC 2297. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Applicant provides guidance for the above noted antibody but provides no guidance as to what modifications or structure are important for the predictable function of any other antibody. Very different structures may be found on antibodies with the same specificity. For example, very different V_H chains can combine with the same V_L chain to produce antibody binding sites with nearly the same size, shape, antigen specificity, and affinity.

A similar phenomenon can also occur when different V_H sequences combine with different V_L sequences to produce antibodies with very similar properties. These observations indicate that divergent variable region sequences, both in and out of complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. Conversely, similar structure may be found on antibodies having different specificities.

In the absence of any guidance other than to the use of antibody 97A6 produced by hybridoma deposited as No. DSM ACC 2297, one would not know or be able to predict what structure or modifications were important and the amount of experimentation required to determine same would be undue.

Note that an enabling disclosure for the preparation and use of only a few analogs of a product does not enable all possible analogs where the characteristics of the analogs are unpredictable. Accordingly, the art indicates that it would require undue experimentation to formulate and use a successful antibody other than antibody 97A6 produced by hybridoma deposited as No. DSM ACC 2297 as recited in the instant invention without the prior demonstration of specific limitations that have not been recited. Amgen Inc. v. Chugai Pharmaceutical Co. Ltd. (18 USPQ 2d 1027 (CAFC 1991)).

14. Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabled for the claimed monoclonal antibodies because the instant specification is not in compliance with the biological deposit rules. Claim 7 is directed to antibody 97A6 produced by hybridoma deposited as No. DSM ACC 2297 which have not been deposited under the provisions of the Budapest treaty. Furthermore, filling of an affidavit or declaration by Applicant or assignee or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this Application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. Specifically the disclosure does not include the required statement regarding replacement. See page 5 lines 1-4. Please add.

Without such a statement, it would be impossible for the skilled artisan to practice the invention of claim 7 because other clones made from the source material have no predictable reasonable expectation of success of being identical to the instantly claimed monoclonal antibodies.

Please note: Applicant's disclosures only monoclonal antibody 97A6 produced by the hybridoma deposited under No. DSM ACCC 2297, therefore art has been applied accordingly.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

I. Claims 1, 5-7, 10-12, and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Buhring (US Patent #6,323,321) as evidenced by Blom et al. (European Journal of Immunology, 1992, Vol.22, No.8, pages 2025-2032) Abstract Only and Hermine et al. (Blood, 1992, Vol. 80, No.12, pages 3060-3069) Abstract Only.

Buhring discloses monoclonal antibody 97A6 produced by the hybridoma deposited under No. DSM ACCC 2297. The antibody is taught to be useful in antigen (surface structure) binding on various cell lines including the megakaryocytic cell line UT-7. See table 1 and column 1 lines 36-39.

In a preferred embodiments the antibody is linked/joined to a fluorescent maker and used in ELISA procedures (immunological detection). Column 2 lines 9-17. In one instance blood samples are screened for antigen binding with the 97A6 antibody. See column 2 lines 59-62. The 97A6 antibody was determined to be of and IgG1 isotype or belonging to the IgG1 immunolglobulin class (not an IgE). Column 3 lines 28-39.

The patent is silent with respect to the antibody binding basophil cells, mast cells, and precursors of these cells. However the antibody was shown to bind cell lines (UT-7 and KU.812), which include the basophil and mast cell type. The prior art teaches that the cell lines which bound antibody 97A6 include mast and basophil cells. Hermine et al. disclose the UT-7 cell line having basophil cells while Blom et al. disclose that the KU812 cell line has mast and basophil cells. Therefore this limitation is inherent to the patent to Buhring.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

I. Claims 2-4, 8-9, and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Buhring (US Patent #6,323,321) in view of Irsch et al. (WO 97/46880).

Buhring differs from the instant invention in not specifically teaching basophil and/or mast cell detection, isolation, quantification, and activation in hematopoiesis.

However, Irsch et al. teach methods for diagnosis from patient's hematopoietic cells. See page 2 lines 29-32 and page 3 lines 3-7. The method separates (isolates) antigen bound cells. Page 5 lines 24-31. Cell analyses and quantification is taught on page 11 lines 10-21. Basophil cell activation or effector cell such as basophilic granulocytes are shown to be useful in positively diagnosis of allergies. See page 11 lines 22-29.

Therefore, it would have been obvious at the time the invention was made to a person having ordinary skill in the art to utilize the reagents and methods taught by Buhring to detect, isolate and quantify hematopoiesis in activated cells like basophils as taught by Irsch et al. because Irsch et al. taught that allergen binding cells such as CD38 (basophilic granulocytes) were useful in allergic patient testing. Page 18 through page 19.

17. For reasons aforementioned, no claims are allowed.

18. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 872-9306, which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to Group 1600 whose telephone number is (571) 272-1600.

Lisa V. Cook
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3/2/04

LONG V. LE
SUPERVISORY PATENT EXAMINER
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